ICAPI: Providing Animals With a Formal Voice at the ICH

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International Council for Animal Protection (ICAP)

International Council on Animal Protection

representing 30 million supporters worldwide

- Asia:
  - Japanese Anti-Vivisection Association
- Europe:
  - British Union for the Abolishment of Vivisection
  - Eurogroup for Animal Welfare
  - European Coalition to End Animal Experiments
- North America:
  - Animal Alliance of Canada
  - Doris Day Animal League
  - Humane Society of the United States
  - People for the Ethical Treatment of Animals
  - Physicians Committee for Responsible Medicine

Representation at the OECD

- **ICAPO** = **I**nternational **C**ouncil on **A**nimal **P**rotection in **O**ECD Programmes

- ICAPO has "invited expert" status at the following OECD meetings:
  - National Coordinators of the OECD Test Guidelines Program
    - Nearly 100 OECD TGs "on the books," of which nearly 1/2 are animal tests
  - OECD Task Force on Endocrine Disrupters Testing + Assessment
    - Developing strategies + methods to test chemicals for hormonal effects
  - OECD Task Force on Existing Chemicals
    - Part of an international effort to test 2,800+ "high production volume" chemicals

- ICAPO has formally requested admission to the OECD Joint Meeting

- ICAPO operates under a confidentiality restriction at OECD

ICAPO Timeline

- April 2001: Formally requested NGO status (alongside industry, trade + environmental stakeholders)
- Jan. 2002: Submitted comments on draft GD on validation and regulatory acceptance
- March 6-8, 2002: Participated in Stockholm conference on validation and regulatory acceptance (by invitation only)
- March 26, 2002: Formally recognized as “invited experts” by OECD
- April 19, 2002: Submitted comments on draft phototoxicity TG (432)
- May 27–28, 2002: Participated in meeting of Task Force on Existing Chemicals, Paris

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- April 12-14, 2005: Participated in the meeting of the National Coordinators of the TG Programme, Paris

Representation at ICH?

- ICAPI = **I**nternational **C**ouncil on **A**nimal **P**rotection at **I**CH
- Participate in Steering Committee meetings when Safety or other animal testing guidelines are being discussed
- Attend EWG meetings for any guidelines containing animal testing
- Support incorporation of "3Rs" of reduction, refinement + replacement of animal testing into ICH guidelines + standards
  - Bring validated models to light + arrange access to the data required for consensus on validation
  - Facilitate harmonisation with other international + national regulatory bodies (e.g., OECD)
  - Submit technical comments on draft guidelines

ICH's Mission & Process

Terms of Reference

"..To facilitate the adoption of new or improved technical research and development approaches which update or replace current practices, where these permit a more economical use of human, **animal** and material resources, without compromising safety.." *[emphasis added]*

Harmonisation of Guidelines

"Transition to technically improved testing procedures: Proposals for action to facilitate the replacement of currently established testing procedures to more efficient and economical methods where these provide equal or better assurance of the safety and/or quality of new drug products."

Examples from ICH Guidelines

Progress

- S2: Genotoxicity: Two tests of standard battery are *in vitro*
- S4: Single Dose Toxicity Tests (LD50) deleted in 1991

Opportunities for Future Progress

- S1: Rodent carcinogenicity studies call for irrelevantly high exposure levels
- S5: Separate male fertility study could be deleted since histopathological examination of reproductive organs in repeated-dose toxicity studies may be more sensitive, so these tests could be combined
- S7/M3: Human microdosing and experimental medicine guidelines needed
- Lack of guidelines addressing non-routine tests with validated non-animal alternatives such as phototoxicity and human-based pyrogenicity

Animal Testing

- Decades-old tests that could not be validated today

- Not reliably predictive of human responses, esp. for different patient populations
  - Species variation and extrapolation
  - Poor disease models
  - Confounding effects of laboratory confinement, stress, environment, food, and so on
  - Repeatability/reproducibility

- Expensive, time-consuming, and not amenable to high throughput

- Attempting to translate research from animals to humans not as efficient as studying humans directly

Animals in the "Critical Path"

Assessing Safety

- Animal toxicology is "laborious, time-consuming, requires large quantities of product, and may fail to predict the specific safety problem that ultimately halts development." - FDA Critical Path report, 3/04

Demonstrating Medical Utility (efficacy)

- "Currently available animal models…have limited predictive value in many disease states" - FDA Critical Path report, 3/04

Resulting in…

Missed opportunities

- "How fortunate we didn't have these animal tests in the 1940s, for penicillin would probably never have been granted a license, and possibly the whole field of antibiotics might never have been realized." – Sir Alexander Fleming

Missed problems

- Animal studies found that COX-2 inhibitors have a ***protective*** effect on cardiovascular health

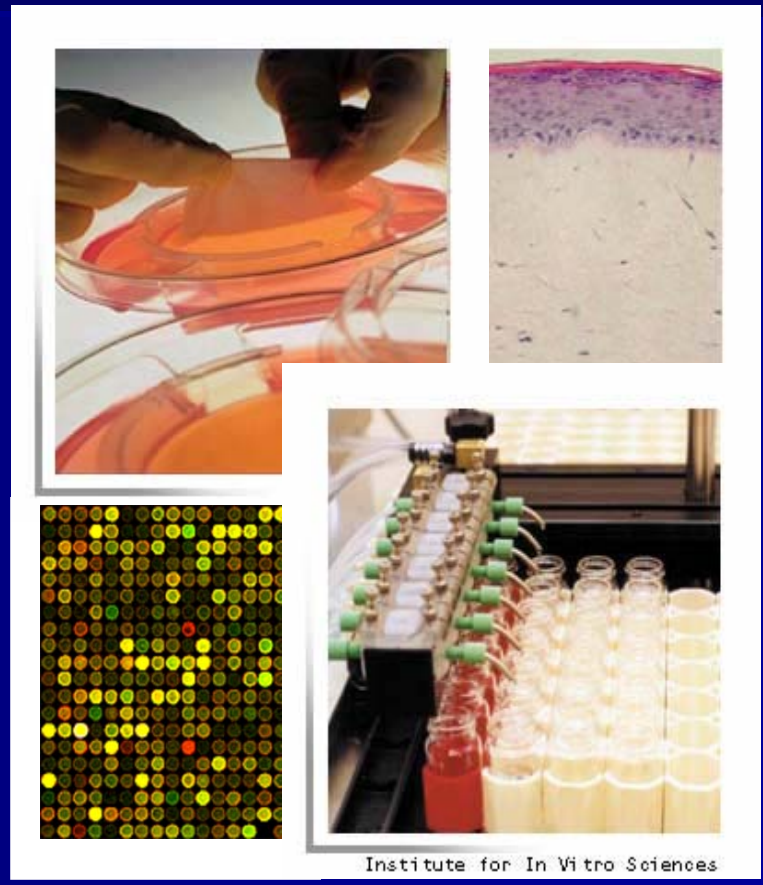
Human-based Research

Target discovery

- Genomics/proteomics profiles of human tissues (e.g., diseased vs. normal)
- Epidemiology with genetic analysis

Safety and efficacy testing

- *In vitro* technologies (tissue cultures, physicochemical)
- Genomics/proteomics/imaging biomarkers in microdosing and experimental medicine trials
- Predictive toxicology and efficacy based on human molecular biology & chemical databases, QSARs, other computer modeling and simulation



Advantages of Alternatives

- Faster results
- Less expensive
- Greater repeatability/reproducibility
- Able to be automated/labor-saving
- Amenable to high throughput
- Species-relevant and thus more predictive (if developed correctly)
- Enable earlier incorporation of safety testing and thus better portfolio management
- Less paperwork/don't require animal care and use committee approval
- Less exposure of personnel to animals and diseases
- More humane/less controversial

Animal Testing & Harmonization

Requirements of EU Directive 86/609

Requires the use of non-animal tests in place of animal tests whenever validated alternatives are available

7th Amendment to the Cosmetics Directive

EU ban on animal testing of cosmetics ingredients phasing in from 2009 to 2013 instigating the development/validation of many new non-animal tests

→ Imminent major harmonization issue for every industry that conducts animal testing